REMARKS/ARGUMENTS

Prior to the present amendments, Claims 1-39 were pending in this application. Claims 3-6 and 16-39 were withdrawn from consideration, Claims 1, 2, and 7-15 were rejected. Claims 1-6 and 16-39 have been canceled, and Claims 7 and 8 have been amended. Support for the recitation of an extracellular domain sequence from within SEQ ID NO 32 is, for example, in paragraphs [0113], [0116], and [0118] of the specification. The amendments to the specification are of formal nature and correct obvious typographical errors, and update the status of certain parent applications. The amendments to the specification and claims do not add new matter.

Detailed Action

Re. 2 Applicants note the finality of the restriction requirement. Accordingly, the invention of Group VI (Claims 1-2 and 6-15) and the species of rheumatoid arthritis are under examination. Applicants specifically reserve the right to petition the Director to review the restriction requirement pursuant to 37 C.F.R. §1.144, but elect to defer the filing of a petition until after final action on or allowance of claims to the invention elected.

Re. 5 Applicants were requested to update the status of parent application U.S. Patent Application Serial Nos. 09/380,138 and 09/953,499 on page 1 of the specification. The foregoing amendments include the requested updates.

Re. 6 The title of the invention was held not descriptive, and Applicants were requested to submit a new title that is clearly indicative of the invention to which the claims are directed. Applicants were further cautioned to avoid the use of "novel" in the title. The foregoing amendments to the specification include a new, specific title, which does not include the term "novel."

Re. 8 The Examiner has pointed out certain discrepancies between Figures 25-26 and the figure legends describing these figures. The foregoing amendments to the figure legends, which are fully supported by the Figures and by paragraph [0456] of the specification, eliminate the discrepancies.

Re. 9 Claims 7-11 were objected to because claim 7 depended from non-elected Claim 4. Claim 7 has been rewritten as an independent claim, which obviates this objection.

Re. 11 Claims 9-11 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. In particular, the Examiner noted that the "antagonist" recited in Claim 7 had no antecedent basis in non-elected base Claim 4. Since Claim 7 as currently amended no longer recites an "antagonist," this rejection is believed to be moot.

Re. 13 Claims 1-2 and 7-15 were rejected under 35 U.S.C. §112, first paragraph, since the specification allegedly does not reasonably provide enablement for the treatment of "any inflammatory disorder," as claimed. The Examiner acknowledges that STIgMA is disclosed to be involved in chronic inflammation (Example 24 and 25) based on the expression of STIgMA in inflamed synovium (page 11, paragraph [0087]), and cites Walker (Biochimica et Biophysicz Acta, 1574 (20020 387-390) teaching that "high expression of STIgMA mRNA was found in the synovium of patients with rheumatoid arthritis when compared its expression to the expression patterns of genes with known functions." The Examiner further cites the conclusion of Walker that "better understanding of Z391g (STIgMA) gene may help us mediate the adverse effects of complement and activated macrophages in rheumatoid arthritis," and notes that "mRNA STIgMA abundance correlates with the protein expression using polyclonal antibody 6F1." However, the claims are rejected since although a correlation between the levels of STIgMA in activated macrophages and synovicytes in inflamed joints "may provide an indication that particular compounds/compositions are appropriate to target *for further experimental consideration*" (emphasis original), the specification "does not appear to have provided the skilled artisan with sufficient guidance and support as to how to extrapolate the development of effective *in vivo* human therapeutic methods, commensurate in scope with the claimed invention." The Examiner adds that the "specification fails to provide any guidance and direction as to how the skilled artisan can make . . , antagonists of a native sequence STIgMA polypeptide that can be used to treat an inflammatory disorder." The Examiner additionally cited Kahan as allegedly teaching that there is not in vitro immune assay that would predict or correlate with in vivo immunosuppressive efficacy, therefore, there is no surrogate immune parameter as a basis of immunosuppressive efficacy and/or for does extrapolation from in vitro systems to in vivo conditions. Citing Ex parte Krepelka, the Examiner concludes that substantiating evidence in the from of animal tests, which constitute recognized screening

procedures with clear relevance to efficacy in humans, would be required to support the claimed invention.

Claims 1 and 2 have been canceled. The rejection of the remaining claims is respectfully traversed.

The invention claimed in the present application concerns the use of certain well specified STIgMA immunoadhesins for the treatment of inflammatory conditions. In particular, as a result of an election of species requirement, the claims are examined to the extent that they relate to the treatment of rheumatoid arthritis. The main reason for the rejection appears to be that, according to the Examiner, the specification contains only *in vitro* data indicating the involvement of STIgMA in chronic inflammation, which, in the absence of "substantiating evidence in the form of animal tests," is insufficient to support the claimed invention. Applicants submit that Examples 24 and 25 of the specification provide overwhelming evidence supporting the involvement of STIgMA in chronic inflammation, and therefore the present rejection should be withdrawn.

Example 24 provides data demonstrating that: (1) the expression of STIgMA in macrophages significantly increased in the presence of pro-inflammatory cytokines; (2) high expression levels of STIgMA mRNA were found in alveolar macrophages obtained from lung autopsy of human patients with *pneumonia* and *chronic asthma*, and in Kupffer cells of a human patient with *chronic hepatitis* (Figures 63A-F); (3) high expression levels of STIgMA mRNA were found in synovial cells obtained from a human patient with *osteoarthritis* (Figures 64A-D); (4) expression of STIgMA protein was confirmed in the synovium of a human patient with *rheumatoid arthritis*, while STIgMA was absent in control synovium (Figures 65A-D); (5) STIgMA mRNA levels were 16 fold over normal in colon tissue obtained from a human patient with *ulcerative colitis*, 5 fold over normal in colon tissue obtained from a human patient with *Crohn's disease*, and 14 fold over normal in lung tissue from a human patient with *chronic occlusive pulmonary disease (COPD)* (Figure 69).

Example 25 discloses data obtained in a well known mouse model of arthritis In particular, the experimental data set forth in Example 25 show that murine STIgMA is highly expressed in macrophages and synoviocytes in inflamed joints of mice with collagen-induced arthritis, and that systemic injection of the STIgMA fusion protein muSTIgMA-Fc, into

collagen-induced arthritic mice resulted in a significant reduction in the progression of CIA compared to a control group of mice treated with IgG1 (Figure 71). Thus, the specification does contain actual experimental data in the form of animal tests, which directly support the claimed invention.

The extensive experimental data provided in the specification clearly establish that STIgMA mRNA and protein expression are associated with a large variety of inflammatory conditions in humans and demonstrate that an inflammatory condition characterized by elevated STIgMA levels (rheumatoid arthritis) can be successfully treated by administration of a STIgMA-Ig immunoadhesin in a relevant animal model. Therefore, the Examiner's assertions about "the limited working examples," and the alleged lack of animal tests are believed to be misplaced. Applicants submit that the data and general teaching provided in the specification at the priority date of this application fully enabled a person of ordinary skill to practice the claimed invention within the full scope of the claims pending without undue experimentation, and respectfully request the reconsideration and withdrawal of the present rejection.

Re 14. Claims 1-2 and 7-15 were rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in the possession of the claimed invention at the time the application was filed.

According to the rejection, "[n]either the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the [claimed] genus" of STIgMA antagonists, immunoadhesins, STIgMA extracellular domain sequences, Ig constant domain sequences, etc.

Claims 1 and 2 have been canceled. The rejection of the remaining claims is respectfully traversed.

The claims currently pending are directed to the treatment of inflammatory conditions with immunoadhesins comprising an extracellular domain sequence of a STIgMA polypeptides of SEQ ID NO: 32. Immunoadhesins were well known in the art at the priority date of the present application and are described in the specification, for example, in paragraphs [0160], [0402]-[0408], [0418]-[0422] and in Example 25. The extracellular domain within SEQ ID NO: 32 is clearly defined, *e.g.*, in paragraph [0118]. Since the claimed genus is described by well-

defined structural features, in view of this teaching and general knowledge in the art, at the time the application was filed one of ordinary skill would have clearly appreciated that Applicants were in the possession of the claimed invention.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Re 15. Claim 1 was rejected as "not patentably distinct" over Claims 1-8 of commonly assigned U.S. Patent Application Serial No. 10/265,542, under the judicially created doctrine of obviousness-type double patenting. Without acquiescing to the rejection, Claim 1 has been canceled, which moots the present rejection.

Re 17. Claim 1 was rejected under the judicially created doctrine of obviousness-type double patenting as "unpatentable" over Claims 1-8 of U.S. Patent Application Serial No. 10/265,542. Without acquiescing to the rejection, claim 1 has been canceled, which moots the present rejection.

Re 18. Claim 1 was provisionally rejected under 35 U.S.C. §103(a) as allegedly obvious over copending U.S. Patent Application Serial No. 10/265,542, which has common inventors with the instant application. Without acquiescing to the rejection, claim 1 has been canceled, which moots the present rejection.

All claims pending in this application are in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39766-0100 P1**).

Respectfully submitted,

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By: _____
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